WHAT IS CLAIMED IS:

1. A composition comprising a preselected polypeptide capable of participating in an activity, said preselected polypeptide having at least a first and a second position the relative proximities of which are capable of changing in relation to the activity of said preselected polypeptide, said composition comprising said preselected polypeptide or a fragment thereof and having at least a first and a second detectably interacting proximity-sensor peptide located in the amino acid backbone of said composition proximal to said first and second positions, respectively, wherein said relative proximities of said positions in said composition are capable of changing in relation to the activity of said composition.

2. The composition of claim 1 wherein said activity is selected from the group consisting of intramolecular interactions, intermolecular interactions, interaction with a ligand, interaction with a substrate, change in dielectric constant, change in pH, change in protein folding, post-translational modification, and modification of a residue.

3. The composition of claim 2 wherein said modification of a residue is selected from the group consisting of phosphorylation and dephosphorylation.

4. The composition of claim 1 wherein said preselected polypeptide is a protein kinase or a protein kinase substrate.

5. The composition of claim 4 wherein said protein kinase substrate is Crk-II.

6. The composition of claim 1 wherein said first interacting proximity-sensor peptide is at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said preselected polypeptide or fragment thereof, the C-terminus of which is peptide bonded to the N-terminus of said second interacting proximity-sensor peptide.

7. The composition of claim 1 wherein said preselected polypeptide is recombinant.

8. The composition of claim 1 wherein said preselected polypeptide has an N-terminal cysteine and a C-terminal $^{\alpha}$thioester.

9. The composition of claim 1 wherein said at least two interacting proximity-sensor peptides comprise a FRET pair.

10. The composition of claim 9 wherein said FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and

fluorescein, EDANS and DABCYL, BODIPY fluorescein and BODIPY fluorescein, β-phycoerythrin and CY5, and pyrene and coumarin.

11. The composition of claim 10 wherein said FRET pair is tetramethylrhodamine and fluorescein.

12. The composition of claim 1 wherein said interacting proximity-sensor peptide is a synthetic oligopeptide comprising a fluorescent amino acid derivative.

13. The composition of claim 1 as set forth in Figure 5A (SEQ ID No:8).

14. The composition of claim 1 comprising a third interacting proximity-sensor peptide.

15. A method for measuring changes in the relative proximity between at least a first position and a second position in a preselected polypeptide, said polypeptide capable of participating in an activity, said changes related to the activity of said polypeptide, comprising the steps of:

(a) providing the composition of claim 1;

(b) subjecting said composition to conditions inducing said activity; and

(c) measuring said changes in relative proximity of said first and second detectably interacting proximity-sensor peptides in said composition.

16. The method of claim 15 wherein said conditions inducing said activity are selected from the group consisting of exposing said composition to a substrate, exposing said composition to a ligand, exposing said composition to a binding partner, exposing said composition to conditions in which said composition is acted upon by an enzyme, post-translational modification, change in pH, change in dielectric constant, and change in protein folding.

17. The method of claim 16 wherein said measuring said changes is performed by a method selected from the group consisting of fluorescence spectroscopy, nuclear magnetic resonance spectroscopy, electron spin resonance spectroscopy, ultraviolet/visible spectroscopy, and extent of cross-linking by cross-linking agents.

18. A method for identifying an agent capable of modulating the activity of a preselected polypeptide, said polypeptide capable of participating in an activity, said activity detectable by changes in the relative proximity among at least a first position and at least a second position in said preselected polypeptide, comprising the steps of:

(a) providing the composition of claim 1;

(b) subjecting said composition to conditions inducing said activity in the presence and absence of said agent;

(c) measuring said changes in relative proximity of said first and second detectably interacting proximity-sensor peptides in said composition in the presence and absence of said agent; and

(d) identifying said agent affecting said changes as capable of modulating said activity.

19. The method of claim 18 wherein said activity is a consequence of intramolecular interactions, intermolecular interactions, interaction with a ligand, interaction with a substrate, change in dielectric constant, change in pH, change in protein folding, post-translational modification, or modification of a residue.

20. The method of claim 19 wherein said post-translational modification is phosphorylation and dephosphorylation.

21. The method of claim 18 wherein said preselected polypeptide is a protein kinase or a protein kinase substrate.

22. The method of claim 21 wherein said protein kinase substrate is Crk-II.

23. The method of claim 18 wherein said first interacting proximity-sensor peptide is at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said recombinant portion, the C-terminus of which is peptide bonded to the N-terminus of said second interacting proximity-sensor peptide.

24. The method of claim 18 wherein said preselected polypeptide is recombinant.

25. The method of claim 18 wherein said polypeptide has an N-terminal cysteine and a C-terminal $^{\alpha}$thioester.

26. The method of claim 18 wherein said at least two interacting proximity-sensor peptides comprise a FRET pair.

27. The method of claim 26 wherein said FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and fluorescein, EDANS and DABCYL, BODIPY FL fluorescein and BODIPY fluorescein, β-phycoerythrin and CY5, and pyrene and coumarin.

28. The method of claim 27 wherein said FRET pair is tetramethylrhodamine and fluorescein.

29. The method of claim 18 wherein each of said interacting proximity-sensor peptides is a synthetic oligopeptide comprising a fluorescent amino acid derivative.

30. A method for preparing a composition comprising a preselected polypeptide capable of communicating changes in the relative proximity among at least one first position and at least one second position in said preselected polypeptide, said polypeptide capable of participating in an activity, said changes related to the activity of said preselected polypeptide, comprising the steps of:

(a) providing at least a first interacting proximity-sensor peptide and a second interacting proximity-sensor peptide, each of said peptides having a detectably interacting proximity-sensitive moiety present therein, said moieties capable of communicating changes in said relative proximity;

(b) providing at least one recombinant polypeptide or portion of said preselected polypeptide, said recombinant portion having an N-terminal cysteine, a C-terminal thioester, or the combination thereof;

(c) ligating said at least one recombinant polypeptide or portion thereof and said at least first and second interacting proximity-sensor peptides into an amino acid backbone at said first

position and at least one second position to provide a composition comprising said preselected polypeptide, such that in said composition said relative proximities of said positions of said second interacting proximity-sensor peptides are capable of changing in relation to the activity of said composition.

31. The method of claim 30 wherein said interacting proximity-sensor peptide has an N-terminal cysteine, a C-terminal thioester, or the combination thereof.

32. The method of claim 30 wherein said amino acid backbone is comprises a first interacting proximity-sensor peptide at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said recombinant portion, and the C-terminus of which is peptide bonded to the N-terminus of said second interacting proximity-sensor peptide.

33. The composition shown in Figure 5A (SEQ ID No:8).

34. A method for measuring changes in the relative proximity between at least a first position and a second position in Crk-II, said changes related to the activity of Crk-II, comprising the steps of:

(a) providing the composition of SEQ ID No:8;

(b) subjecting said composition to conditions inducing said activity; and

(c) measuring said changes in relative proximity of said first and second detectably interacting proximity-sensor peptides in said composition.

35. The method of claim 34 wherein said conditions inducing said activity is phosphorylation and dephosphorylation.

36. The method of claim 35 wherein said phosphorylation and dephosphorylation is induced by c-Abl or the epidermal growth factor receptor.

37. The method of claim 34 wherein said measuring said changes is performed by fluorescence spectroscopy.

38. A method for identifying an agent capable of modulating the activity of Crk-II or modulating the activity of a protein kinase capable of phosphorylating Crk-II, said activity ~~detectable by~~ changes in the relative proximity among at least a first position and at least a second position in Crk-II, comprising the steps of:

(a) providing the composition of SEQ ID No:8;

(b) subjecting said composition to conditions inducing said activity in the presence and absence of said agent;

(c) measuring said changes in relative proximity of said first and second detectably interacting proximity-sensor peptides in said composition in the presence and absence of said agent; and

(d) identifying said agent affecting said changes as capable of modulating said activity.

39. The method of claim 38 wherein said phosphorylation and dephosphorylation is induced by c-Abl or the epidermal growth factor receptor.

40. A method for identifying an agent capable of modulating the activity of a protein kinase target, or modulating the activity of a protein kinase capable of phosphorylating said target, said activity detectable by changes in the relative proximity among at least a first position and at least a second position in said target, comprising the steps of:

(a) providing a target composition comprising said preselected polypeptide or a fragment thereof, and having at least a first and a second detectably interacting proximity-sensor peptide located in the amino acid backbone of said composition proximal to said first and second positions, respectively, wherein said relative proximities of said positions in said composition are capable of changing in relation to the activity of said composition;

(b) subjecting said composition to conditions inducing said activity in the presence and absence of said agent;

(c) measuring said changes in relative proximity of said first and second detectably interacting proximity-sensor peptides in said composition in the presence and absence of said agent; and

(d) identifying said agent affecting said changes as capable of modulating said activity.

41. The method of claim 40 wherein said protein kinase is c-Abl or epidermal growth factor receptor.

42. The method of claim 40 wherein said protein kinase target is Crk-II.

43. The method of claim 40 wherein said first interacting proximity-sensor peptide is at the N-terminus, the C-terminus of which is peptide-bonded to the N-terminus of said recombinant portion, the C-terminus of which is peptide bonded to the N-terminus of said second interacting proximity-sensor peptide.

44. The method of claim 40 wherein said preselected polypeptide is recombinant.

45. The method of claim 40 wherein said polypeptide has an N-terminal cysteine and a C-terminal $^{\alpha}$thioester.

46. The method of claim 40 wherein said at least two interacting proximity-sensor peptides comprise a FRET pair.

47. The method of claim 46 wherein said FRET pair is selected from the group consisting of fluorescein and tetramethylrhodamine, IAEDANS and fluorescein, EDANS and DABCYL, BODIPY FL fluorescein and BODIPY fluorescein, β-phycoerythrin and CY5, and pyrene and coumarin.

48. The method of claim 47 wherein said FRET pair is tetramethylrhodamine and fluorescein.

49. The method of claim 40 wherein each of said interacting proximity-sensor peptides is a synthetic oligopeptide comprising a fluorescent amino acid derivative.

50. The composition shown in SEQ ID No:9.

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